Pre-hospital risk stratification in suspected Non ST-elevation acute coronary syndrome

SUMMARY AND CONCLUSIONS

Until now, complete risk stratification in patients with suspected NSTE-ACS is performed in the hospital. However, since point-of-care troponin assessment has been developed, risk stratification is nowadays also performable outside the hospital. This thesis addresses the feasibility of pre-hospital risk stratification in suspected NSTE-ACS. The goals of this thesis were to investigate how low-risk patients can be accurately identified by paramedics, to assess the healthcare utilization in those patients and to evaluate whether patients at high-risk for revascularization can be identified.

In **chapter 1**, a brief introduction about the subject and the background of the thesis is given. Suspected NSTE-ACS is a common reason for emergency department presentation and requires fast risk stratification. Further research is needed to assess whether risk stratification with subsequent treatment decisions is feasible in the pre-hospital setting.

The first phase of the Famous Triage research project is reported in **chapter 2**. This was the first study in which paramedics assessed a pre-hospital HEART score. In 600 patients with suspected NSTE-ACS the HEAR components of the HEART score were prospectively assessed by paramedics. Blood samples were collected at time of inclusion and troponin assessment was performed in the hospital. A total of 140 patients (23%) were classified as low, 341 (57%) as intermediate and 119 (20%) as high-risk patients. Occurrence of MACE within 30 days was 3%, 19% and 45%, respectively ($p < 0.001$). There were no deaths in the low-risk group. AUC of the pre-hospital HEART score for predicting MACE was 0.77 (95% CI 0.73 – 0.81). The importance of this study lies primarily in proving the feasibility of pre-hospital HEAR(T) scoring by paramedics.

For the second phase of the Famous Triage research project, a pre-hospital point-of-care troponin was introduced in the ambulance. **Chapter 3** describes the main outcomes of this study. In 700 patients with suspected NSTE-ACS risk stratification was performed by paramedics. A total of 172 patients (25%) were stratified as low risk and 528 patients (75%) as intermediate to high-risk. MACE occurred in 5 patients in the low-risk group (3%) and in 111 (21%) patients at intermediate or high risk ($p < 0.001$). There were no deaths in the low-risk group and the occurrence of acute myocardial infarction in this group was 1%. In the high-risk group 6 patients died (1%) and 76 patients had myocardial infarction (14.4%). Conclusion was that pre-hospital risk stratification by paramedics is accurate, but to decrease MACE in the low-risk group further training of paramedics and a second troponin assessment when measurement was shortly after complaint onset are needed.

In **chapter 4** we assessed the added value of the troponin component to the HEART score. Mean HEAR score was 4.5 ± 1.6, mean HEART score was 4.7 ± 1.7. Using the HEAR score, a total of 183 patients (26%) were stratified as low risk, whereas using the HEART score, 172 patients (25%) were stratified as low risk (p = 0.001). In both low-risk groups, there were no deaths within 45 days. Using HEAR, MACE occurred in 13 patients (7%) in the low-risk group, whereas using HEART, MACE occurred in 5 patients in the low-risk group (3%, p <0.001). The use of HEART (AUC 0.74) obtained a higher predictive value compared to HEAR (AUC 0.65, p <0.001) for MACE. Conclusion was that in patients with suspected NSTE-ACS, the pre-hospital troponin component of the HEART score has important added predictive value.

Whether a pre-hospital HEART score is equally accurate with using point-of-care or high sensitive troponin is investigated in **chapter 5**. In 689 consecutive patients with suspected NSTE-ACS, point-of-care troponin and laboratory high-sensitive troponin were measured in pre-hospital derived blood. For every patient the HEART score with both point-of-care troponin (HEART-POC) and high sensitive troponin (HEART-hsTnT) was determined. 163 (24%) Patients were considered low-risk by using HEART-hsTnT and 170 (25%) by using HEART-POC. Although high sensitive versus POC troponin scoring was different in 130 (19%) of patients, in 678 (98%) patients risk classification in low versus intermediate-high risk was similar. The predictive values of HEART-POC versus HEART-HsTnT was also similar (AUC 0.75 versus 0.76, p = 0.241). Conclusion was that POC troponin measurement suffices for pre-hospital risk stratification in suspected NSTE-ACS.

Because the HEART score was originally validated in the hospital setting we compared the pre-hospital HEART score with the in-hospital HEART score in **chapter 6**. In 699 patients with suspected NSTE-ACS, the HEART score was independently prospectively assessed in the pre-hospital setting by ambulance paramedics and in the hospital by physicians. In 516 (74%) patients pre-hospital and hospital risk classification was similar, in 50 (7%) pre-hospital risk classification was false negative (45 days mortality 0%) and in 133 (19%) false positive (45 days mortality 1.5%). Occurrence of MACE was comparable in pre-hospital and hospital low-risk patients (2.9% versus 2.7%, p = 0.9). Predictive values of both pre-hospital and hospital acquired HEART scores were high, although the AUC of hospital acquired HEART score was higher (0.84 vs 0.74, p <0.001). Disagreement was primarily caused by different scoring of history and risk factors and therefore additional training may improve pre-hospital scoring.

If low-risk patients do not need to be transferred to the hospital anymore in the future, there might be a reduction in healthcare utilization (and costs). In **chapter 7** we assessed the diagnostics in pre-hospital low-risk patients and the contribution of those

diagnostic results in the healthcare process. 84% of patients was discharged within 12 hours. Repeated electrocardiography and routine laboratory measurements, including cardiac markers were performed in all patients. Chest X-ray was performed in 61%, echocardiography in 11% of patients. After additional diagnostics, 2 patients (1%) were diagnosed as non-STEMI, 2 patients (1%) as unstable angina. Other diagnoses were atrial fibrillation (n=1) and acute pancreatitis/cholecystitis (n=2), all other patients had non-specific/non-acute discharge diagnoses. Mean in-hospital costs per patient were €1.580. The estimated yearly acute healthcare costs in low-risk chest pain patients in the Netherlands are €30.438.700.

Beside early identification of low-risk patients, pre-hospital risk assessment could also facilitate faster identification of high-risk patients. In **chapter 8** we investigated whether patients at high risk for early revascularization can be identified in a pre-hospital setting. This was a prospective cohort study including 1289 consecutive patients with suspected NSTE-ACS in which the HEART score including point-of-care troponin was performed by paramedics. Endpoint was revascularization (PCI or CABG) within 30 days of inclusion. A total of 164 patients (13%) received revascularization within 30 days. Of 99 patients (8% of total group) with elevated point-of-care troponin, 49 (49%) received revascularization. Of 180 patients (14%) with high-risk HEART score, 52 (29%) received revascularization. Both elevated troponin (OR 8.7) and high-risk HEART score (OR 3.6) were significantly associated with revascularization after univariate analysis. After multivariate regression analysis elevated point-of-care troponin remained the strongest predictor for revascularization. Possibly, patients with elevated point-of-care troponin benefit from direct transfer to a PCI center.

Until now, all research has been observational. Pre-hospital risk assessment and troponin results have not been implemented in pre-hospital treatment decisions. Because the previous mentioned studies showed feasibility of pre-hospital risk assessment, phase 3 of the Famous Triage study was initiated. In **chapter 9** the rationale and design of this phase are reported. The aim is to further assess whether pre-hospital HEART score management including point-of-care troponin measurement and subsequently not transferring low-risk patients to the hospital is feasible and non-inferior to routine management.